

## Disinfection By-products in Drinking Water: Critical Issues in Health Effects Research

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Use of chemical oxidants such as chlorine, chloramines, chlorine dioxide, and ozone as drinking water disinfectants is a well-established and successful treatment practice to combat waterborne disease. As a result of these practices, the incidence of waterborne disease has been greatly reduced. While the addition of chemical oxidants to drinking water yields a measurable benefit in public health protection, it may also result in the introduction of other potential risks. The chemical oxidants react with naturally occurring organic and inorganic substances to form by-products. These by-products have been shown to produce adverse health effects in laboratory animal studies. In 1979, the U.S. Environmental Protection Agency (EPA) regulated the most prevalent group of by-products, trihalomethanes, as surrogates for the range of by-products that could be formed. This initial regulation triggered substantial research related to the occurrence of disinfection by-products and their potential health effects. The EPA is now in the process of revising and enhancing its regulation of disinfection by-products to include compounds other than trihalomethanes. The European Union directive on drinking water is also under revision, as is the Canadian Drinking Water Safety Act. These regulatory processes require a careful balance of reducing exposure to chemical by-products of disinfection while maintaining control of waterborne pathogens.

The issue of balancing chemical and microbial risks was the topic of a successful conference on the safety of water disinfection organized by the International Life Sciences Institute (ILSI) in 1992. This conference noted that, while the health risks from microbial contaminants in drinking water supplies are substantial as compared with the theoretical risks from chemical by-products, there remains uncertainty as to the actual risks posed by disinfectants and their by-products. During October 1995, ILSI organized a follow-up workshop in Chapel Hill, North Carolina, to examine

the state-of-the-science of the health effects research for disinfection by-products and to determine the priorities for further research. This second workshop provided a forum for scientists from the disciplines of toxicology, chemistry, epidemiology, water treatment technology, public health, and risk assessment to discuss the recent advances in health effects research on disinfection by-products. The workshop sessions addressed recent research findings related to health effects of by-products of both chlorination and alternative disinfectant practices, biologically based risk assessment models, predictive toxicology, epidemiology, drinking water as a complex mixture, new procedures for assessing risk, and priorities for further research.

The following issues reflect the key conclusions and recommendations developed during the final session of the workshop regarding priorities for future research on the health effects of disinfection by-products.

### General Recommendations

Microbial contamination of water supplies poses a clear public health hazard when treatment is inadequate. Any efforts to reduce potential health risks associated with disinfection by-products must not compromise the microbiological quality of drinking water currently achieved through disinfection and physical removal of pathogens.

While available data suggest that the risks from disinfection by-products appear low at the current levels of exposure, the ubiquitous human exposure to these by-products in drinking water raises the concern that even small risks could have public health significance. Therefore, additional research is needed to further investigate whether exposure to disinfection by-products poses a public health risk.

Drinking water research involves a variety of cross-disciplinary issues. Therefore, researchers are encouraged to seek input from and, as appropriate, to collaborate

with scientists in other fields when designing and conducting disinfection by-product research. Such communication will help ensure that the limited resources available for research are wisely targeted.

### Prioritizing Research on Disinfection By-products

Many by-products from the various disinfection processes have yet to be identified. Further analytical research to identify disinfection by-products should focus on low molecular weight compounds (e.g., below 5,000 daltons) that occur in relatively high concentrations, with a particular emphasis on polar compounds, which can now be identified using emerging analytical techniques.

Research efforts should focus on those compounds that appear, based on the available concentration and/or toxicity data, most likely to be of public health concern. Screening processes should be devised to prioritize disinfection by-products for further research based on comparison of specific toxicity and exposure parameters.

A minimum concentration should be established that would serve as a cutoff for research decisions. Disinfection by-products occurring in drinking water at concentrations below this minimum would not be considered a likely public health concern and would not have priority for research.

The suggested approach to prioritizing substances of concern was to compare the estimated human exposure at the 90<sup>th</sup> percentile with the toxic dose in laboratory animals. The substances with the lowest ratios would be considered as highest priorities for further study.

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A full report of the workshop is available through ILSI at 202/659-3306 or [hesi@dc.ilsi.org](mailto:hesi@dc.ilsi.org). Received 18 September 1996; accepted 25 October 1996.

When prioritizing compounds for research, information on a compound's stability or potential for degradation should also be considered to provide perspective on the degree of exposure and the potential public health concern associated with specific disinfection by-products.

Insufficient data are available for many classes of by-products to support predictive structure-activity relationship (SAR) models for use in setting research priorities. However, in a few cases, sufficient data may be available to develop preliminary SAR models for use in hypothesis generation and testing prioritization.

### Hazard Identification/Mechanistic Research

Research to characterize the toxicity of the highest priority disinfection by-products should not be limited to high-dose hazard identification, but rather should focus on determining whether these compounds cause effects at low doses.

In general, sufficient screening-level toxicity data are available for the known by-products of chlorination.

For certain disinfection by-products, mechanistic research will be important to provide a meaningful basis for extrapolating the data below the detection limits of cancer and other toxicological bioassays. Mechanistic research should also be an emphasis in the future to provide a basis for interpreting potential differences among species and designing mixtures and interactions studies.

No further chronic bioassay research on chloroform is necessary because extensive research indicates it is unlikely that chloroform, at the average concentrations found in chlorinated drinking water, poses a significant human health risk.

To provide a meaningful basis for low-dose extrapolation, studies of interactions and mixtures should be predicated on the development and testing of specific hypotheses about how the chemicals in question may be anticipated to interact.

### Epidemiological Studies

Epidemiology should be hypothesis-driven and supported by improved exposure

assessment to enable epidemiological assessment of the total possible risks associated with disinfection by-products from multiple sources and testing of hypotheses for specific by-product classes.

Further epidemiological studies on cancer should concentrate on the relative risk of populations exposed continuously to high and low concentrations of disinfection by-products to help overcome problems of measuring changing exposure over time.

Further epidemiological studies of all endpoints should identify populations exposed to low and high bromide surface waters and brominated disinfection by-products to follow up on toxicological data from laboratory animal studies.

Further epidemiological studies of reproductive outcomes are needed to ensure that such effects are truly associated with disinfectant by-products at environmental exposure concentrations.

### Communication

Communication among the scientific community, decision makers, and the public about the benefits and risks associated with

drinking water disinfection should be improved and should form part of a comprehensive risk management strategy.

Information on how the risk of microbial contaminants compares to the risk posed by disinfection by-products would be useful in a number of developing countries where there is a high level of public concern about these by-products, particularly potentially carcinogenic disinfection by-products in drinking water.

Overall, the workshop provided an important opportunity for scientists from the various disciplines that are concerned with the safety of drinking water to discuss the critical issues in health effects research for disinfection by-products, the current state of the science, and remaining gaps in understanding. It is hoped that the recommendations from this workshop will provide useful guidance to researchers in academic, industrial, and regulatory laboratories as efforts continue to generate the information necessary to ensure the safety of drinking water throughout the world in a cost-effective and timely manner.

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